REMARKS

Claims 1, 4-15, and 43-53 are being examined in this application. Claims 51 and 52 are objected based on formalities. Claims 1, 4-15, and 43-53 stand rejected, under 35 U.S.C. § 112, first paragraph, and claims 1, 4-15, 43, and 51-53 stand rejected under 35 U.S.C. § 102. Claims 1, 4-15, and 43-53 also stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting. Each of these issues is addressed below in the order in which it appears in the Office action.

Amendments

By the present amendment, claims 1, 8, 15, and 51-53 have been amended. The amendment to claim 1 finds support in the specification at page 16, lines 12-13, where mitotic reprogramming media, such as a mitotic cell extract, is defined. This claim has also been amended to clarify that by the use of the term "comprising" in claim 1 Applicants mean "having." In addition, the term "recipient oocyte" in claim 1 has been amended to read "reconstituted oocye," a term that more precisely describes the oocyte and support for which is found in the specification at page 3, line 24, page 51, line 26, and page 57, line 8. Claims 8, 15, and 51-53 are also amended to conform the language of these dependent claims with that of independent claim 1.

No new matter is added by these amendments, and Applicants reserve the right to pursue all canceled subject matter in this or a future, related application.

Claim Objection

Claims 51 and 52 stand objected to as incorrectly reciting "step (b)" when "step (c)" was intended. These claims have been amended to correct this formality.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1, 4-15, and 43-53 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Office acknowledges that Applicants' specification recites a mitotic cell extract, but bases the rejection on the assertion that (pages 4-5):

> a review of the specific teachings in the specification do not clearly describe the structural[ly] elements of this mitotic cell extract or the relevant methods required to practice the methods as broadly claimed. Again, [it] is noted the literal support for the amendment is only as an example and review of the specification does not describe or support the breadth of any cell extract to provide for the removal or addition of "a factor" that would result in a recipient oocyte that develops into a fetus. Mitotic is a broad term encompassing any part of the mitotic cell cycle, and extract is broad [and] encompass[es] any and all types of extraction procedures. There is no specific guidance nor description of the requirements of any specific extract that could be used successfully in the instantly claimed method.
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> In the instant case, Applicants have amended the claims to recite a general example that has literal support in the specification, however have failed to provide any specific description of this embodiment that would be functional in the context of the claimed method.

This rejection is respectfully traversed.

On this issue, the Office is first directed to Applicants' amendment of claim 1. This claim no longer requires the removal of a factor from or addition of a factor to the nucleus, chromatin mass, or chromosome of the permeabilized cell, but instead requires incubation of the permeabilized cell in a mitotic cell extract under conditions that allow chromatin condensation and nuclear envelope breakdown, cell processes triggered by the mitotic cell extract as indicated by the present specification at page 38, line 24 – page 39, line 9 and page 53, lines 1-4.

In addition, on the issue of whether Applicants' specification describes or provides support for the production of mitotic cell extracts that could be used in the presently

claimed method, the Office is directed to Applicants' specification beginning at page 36, line 22 (Example 2). There, the specification provides, in full detail, exemplary methods for producing mitotic cell extracts. These exemplary methods involve techniques for the synchronization of cells in mitosis, cell harvest, pelleting, and washing, followed by lysing of cells by art-recognized methods such as sonication or physical disruption. The lysate may then be centrifuged to remove cell debris and, if desired, membrane vesicles, to produce a mitotic cell extract. These exemplary procedures result in the production of mitotic cell extracts, and no further written description in the specification is necessary to "convey with reasonable clarity to those of skill in the art" that Applicants were "in possession" of this aspect of the invention.

On this issue, the Office is further directed to page 48, line 25 to page 49, line 7 of Applicants' specification where protocols are provided for incubation of permeabilized cells in mitotic cell extracts and page 50, line 17 to page 51, line 17 where results are provided indicating that mitotic cell extract incubation does not induce significant levels of cell death (Table 2). The Office is also directed to page 52, line 12 et seq. and Figures 5 and 6B, where results are presented showing that Applicants' mitotic cell extracts successfully induce chromatin condensation and nuclear envelope breakdown in approximately 80% of treated nuclei (Figs. 5 and 6B). In addition, and very importantly, the Office is directed to page 55, line 10 et seq. where Applicants demonstrate that permeabilized cells incubated in mitotic cell extract and transferred to recipient oocytes developed into 40-day and 40- to 60-day embryos.

In view of these teachings in the specification, the written description rejection should be withdrawn. Applicants have provided in their specification relevant and straightforward methods for producing and using mitotic cell extracts and have demonstrated that these extracts successfully trigger the cellular events of nuclear envelope breakdown and chromatin condensation. It is this function of the extract that is

important to its workability, and not that the extract be derived from cells at one specific stage of the mitotic cell cycle.

In addition, contrary to the Office's position, the case law does not require that one describe the structural elements of a mitotic cell extract. This term is not directed to a genus of unknown members defined by function only and lacking any structural elements. Rather, the mitotic cell extract has a well-defined function in the claims and *is* the structural element -- it is the physical extract prepared from a mitotic cell. This is not equivalent to the broad and undefined class of genes in *Regents of the University of California v. Eli Lilly*, cited by the Office, or the undefined class of "mammalian FGFs" in *Fiddes v. Baird*. As indicated by the Office, in those cases, "one skilled in the art" could not "as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." This is not true of the present case, where one skilled in the art would readily recognize a mitotic cell extract. Neither does *Pfaff v. Wells Electronic, Inc.* support the Office's position, as Applicants have reduced the present invention to practice, a step specified by *Pfaff* to satisfy the written description requirement. Nor are the cases of *Fiers v. Revel*, *Amgen v. Chugai Pharmaceutical Co. Ltd.*, or *In re Wilder* applicable, as Applicants have provided far more than "a mere statement that it is part of the invention and reference to a potential method of identifying it" or an "outline" of "goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate." Applicants have instead described in detail exemplary methods for producing mitotic cell extracts and have demonstrated their successful use for generating cloned embryos.

Finally, contrary to the Office's repeated assertion, Applicants *have* demonstrated that the mitotic cell extracts produced by the methods described in the specification function to generate cloned embryos. Such teachings, set forth at page 55, line 10 et seq and making use of the mitotic cell extracts described in Example 2, clearly satisfy the Office's request for specific guidance or description of the requirements of a specific

extract that could be used successfully in the instantly claimed methods. The written description rejection of claims 1, 4-15, and 43-53 should be withdrawn.

Claims 45-50 also stand rejected, under 35 U.S.C. § 112, first paragraph, as lacking both a written description and lacking enablement. These claims are directed to particular concentration, temperature, and time conditions for streptolysin O incubations. The Office contends that these claims constitute new matter and lack enablement because the specified conditions "are supportive for use at most with the specific cell and other conditions taught in the examples." Applicants respectfully disagree. Applicants' claims require the use of permeabilized cells, and claims 45-50 provide conditions discovered by Applicants to be useful for making those cells. Contrary to the Office's assertion, these conditions are not limited to use with a "specific cell," but can be used to permeabilize a wide variety of cells. With respect to the issue of "other conditions," Applicants are uncertain as to what conditions the Office refers, but assert that, given Applicants' discovery of how to permeabilize cells and the guidance provided in the specification, one skilled in the art would readily be able to carry out the methods covered by claims 45-50 in the absence of undue experimentation. This basis for the § 112 rejection of claims 45-50 should be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 1, 4-15, 43, and 51-53 also stand rejected under 35 U.S.C. § 102(e) as being anticipated by Chapman (U.S. Patent Pub. No 2002/0001842 A1), and claims 1, 7, 9-15, 43, and 51-53 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Machatay (U.S. Patent No. 6,211,429). These rejections are respectfully traversed.

As amended, claim 1 and all dependent claims cover a cloning technique that requires the use of a permeabilized cell "having pores in its plasma membrane or a partial plasma membrane." Nowhere is this claimed invention disclosed by the cited references.

With respect to Chapman, the Office states that this reference is anticipatory because

> the use of comprising [prior to amendment] is broad and open to reasonable interpretation provided by the specification or recognized in the art. In this case the specification supports that a permeabilized cell includes a cell with the plasma membrane completely removed. Further, the methods of Chapman of injection with a needle form a pore through which the cytoplasm is delivered.

This rejection should be withdrawn. First, Applications take issue with the position that "comprising" changes the art-recognized use of the term "pore." A pore is a hole or aperture in a structure, in this case, a plasma membrane. Regardless of the number of pores allowed by the term comprising, some portion of the plasma membrane must be present to allow for the formation of a pore. Nothing about Applicants' specification changes this art-recognized meaning. Nonetheless, claim 1 has been amended to require the use of permeabilized cells "having" pores or a partial plasma membrane to highlight this intended meaning of the term.

The Office's alternative basis for the rejection should also be withdrawn. Chapman's process of microinjecting cytoplasm into a cell does not satisfy the language of either step (a) or step (b) of claim 1. First, the process of injection does not form a pore or create a partial plasma membrane because the entry site of a microinjection needle is closed following removal. Moreover, step (b) of claim 1 requires "*incubating* said permeabilized cell *in* a mitotic cell extract." Chapman's microinjection technique does not involve incubation of a cell *in* any extract, much less one made from a mitotic cell. As recognized by the Office, "the methods of Chapman of injection with a needle form a pore through which the cytoplasm is *delivered*" (Office Action at page 9). This rejection should be withdrawn.

The rejection of claims 1, 7, 9-15, 43, and 51-53 over Machatay (U.S. Patent No. 6,211,429) should also be withdrawn. This rejection similarly focuses on the use of the term "comprising." Again, Applicants point out that this term does not broaden the

claims to encompass cloning techniques that involve an isolated nucleus, but Applicants have nonetheless replaced "comprising" with the term "having" to emphasize this point. Like Chapman, Machatay fails to disclose a permeabilized cell "having pores in its plasma membrane or a partial plasma membrane." Machatay discloses only an isolated nucleus. Further, Machatay fails to discuss incubation of a permeabilized donor cell in a mitotic cell extract, as required by the claims. The § 102 rejection over Machatay should also be withdrawn.

Rejection Based on Double Patenting

Claims 1, 4-15, and 43-53 also stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending applications, Robl (2004/0068760) and Collas (2002/0142397). Applicants recognize that this rejection is provisional, and, upon issuance of claims asserted to be conflicting in either of these applications, Applicants will address this rejection.

Examiner Interview

Should the Office believe that any issues remain in this case, the Examiner is requested to contact Applicants' representative at the telephone number indicated below to arrange for a personal interview.

Conclusion

Applicants submit that this case is now in condition for allowance, and such action is respectfully requested.

Enclosed is a Petition to extend the period for replying to the final Office action for three months, to and including July 11, 2005, and a check in payment of the required extension fee. Also enclosed is a Request for Continued Examination and an Information Disclosure Statement.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 11 July 2005

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